Original research

Five-year results of randomized bioactive versus bare metal coils in the treatment of intracranial aneurysms: the Matrix and Platinum Science (MAPS) Trial

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► Additional material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/neurintsurg-2020-016906).

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Received 19 October 2020
Revised 17 November 2020
Accepted 20 November 2020
Published Online First 9 December 2020

To cite: McDougall CG, Johnston SC, Hetts SW, *et al*. *J NeuroIntervent Surg* 2021;**13**:930–934.

ABSTRACT

Background No randomized trial of intracranial aneurysm coiling has compared long-term efficacy of polymer-modified coils to bare metal coils (BMCs). We report 5-year results comparing Matrix^2 coils to BMCs. The primary objective was to compare the rates of target aneurysm recurrence (TAR) at 12 months. Secondary objectives included angiographic outcomes at TAR or 12 months and TAR at 5 years.

Methods A total of 626 patients were randomized to BMCs or Matrix^2 coils. Detailed methods and 1-year results have been published previously.

Results Of 580 patients eligible for 5-year follow-up, 431 (74.3%) completed follow-up or reached TAR. Matrix^2 coils were non-inferior to BMCs (P=0.8) but did not confer any benefit. Core lab reported post-treatment residual aneurysm filling (Raymond III) correlated with TAR (P<0.0001) and with aneurysm hemorrhage after treatment (P<0.008). Repeat aneurysmal hemorrhage after treatment, but before hospital discharge, occurred in three patients treated for acutely ruptured aneurysms. Additionally, two patients treated for unruptured aneurysms experienced a first hemorrhage during follow-up. All five hemorrhages resulted from aneurysms with Raymond III residual aneurysm filling persisting after initial treatment. After 5 years follow-up, 2/626 (0.3%) patients are known to have had target aneurysm rupture following hospital discharge. The annualized rate of delayed hemorrhage after coiling was 2/398/5=0.001 (0.1%) per year for unruptured aneurysms and 0 for ruptured aneurysms.

Conclusions After 5 years Matrix^2 coils were non-inferior to BMCs but no benefit was demonstrated. Post-treatment residual angiographic aneurysm filling (Raymond III) is strongly associated with TAR (P<0.0001) and post-treatment aneurysmal hemorrhage (P=0.008).

BACKGROUND

The Matrix and Platinum Science Trial (MAPS Trial) was initiated with two objectives. First, this non-inferiority trial was designed to compare results of polymer-modified coils (specifically Matrix^2 coils) versus bare metal coils (BMCs) in the treatment of intracranial aneurysms. Second, the trial was intended to examine the correlation between the initial post-treatment angiographic results according to the modified Raymond Scale[1] and clinical failure. Clinical failure was defined as 'target aneurysm recurrence' (TAR). TAR, a composite clinical endpoint, was said to have occurred if any of the following events were observed: (1) target aneurysm rupture after treatment (first or recurrent), (2) sudden unexplained death, or (3) target aneurysm retreatment. Composite clinical endpoints are a well-accepted standard in other domains of healthcare, for example, in cardiology where the acronym MACE is understood as major adverse cardiovascular event and generally accepted as time to either cardiovascular death or reinfarction or target vessel revascularization for ischemia or stroke, whichever occurs first.[2] Whereas previous randomized trials have compared BMCs to polymer-modified coils,[1 3–7] none have included follow-up beyond 2 years.

METHODS

The trial is registered at ClinicalTrials.gov, Identifier: NCT00396981. Details regarding the materials and methods were published in 2014 along with the findings after 1 year of follow-up.[8] Briefly, this multicenter trial randomized 626 patients undergoing endovascular treatment at 47 centers, 30 US and 17 international, for an intracranial aneurysm to either BMCs or to biopolymer-modified coils (Matrix^2). Both ruptured and unruptured aneurysms were included in the trial. Neuroform stents were allowed at the discretion of the operator.[9] Clinical and imaging follow-up were obtained 1 year after treatment, and clinical follow-up continued until study subjects completed 5 years (1915 days) of follow-up. The primary outcome was TAR at 1 year. Secondary outcomes included neurological assessments at 12 month and TAR at 2, 3 and 5 years. Imaging outcomes were based on blinded independent core lab readings (UCSF Core Lab). Core lab adjudication was available for 488 patients. Imaging follow-up beyond the first year was not required as part of the study.

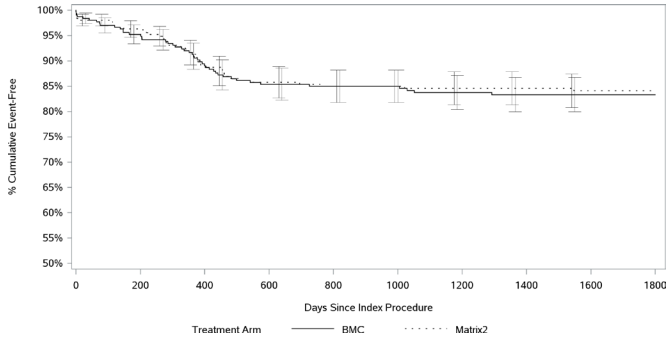

Figure 1 Kaplan–Meier analysis of time to target aneurysm recurrence (TAR). There is no significant difference in time to TAR (upper one-sided 95% CI=4.4%, P=0.8) in comparing outcomes of bare metal coils (BMC) and Matrix^2 coils.

Cross-group comparison of categorical data was evaluated using Chi-squared tests and Fisher's exact test. Time-to-event outcomes were summarized with Kaplan–Meier estimates, and confidence intervals computed with Greenwood's formula. Logistic regression was performed to evaluate the relationship between baseline/post-procedure characteristics and long-term outcome. Variables were selected based on clinical importance. P values were unadjusted for multiplicity. The analysis output was generated using SAS software (SAS Institute Inc., Cary, NC, USA.).

RESULTS

Overall, 626 patients were enrolled in the trial (online supplemental table 1). After 5 years of follow-up there were 46 non-TAR related deaths and 149 patients were lost to follow-up or withdrew from the study leaving 431 patients with completed 5-year follow-up. The median follow-up was 4.8 years for both the BMC and the Matrix^2 groups. Total follow-up in patient years was 2170.6 with 1084.8 and 1085.8 in BMC and Matrix^2 respectively. There was no difference between the two treatment arms with respect to the number of deaths or loss to follow-up. Considering ruptured versus unruptured aneurysms, there were 790.4 patient years of follow-up for 228 patients with ruptured aneurysms and 1515.9 years of patient follow-up for 398 patients with unruptured aneurysms.

Tar in BMC versus Matrix^2

With 5 years of follow-up in all available patients the primary outcome of TAR was observed in 46 (14.4%) and 44 (14.1%) of the BMC and Matrix^2 patients, respectively (figure 1 and online supplemental table 2, P=0.9, Fisher's exact test). Figure 1 highlights the TAR-free survival rate. In raw percentages (online supplemental table 2), ruptures of the target aneurysm ruptured after treatment in 3/315 (1%) BMC and in 2/311 (0.6%) Matrix^2 patients. Retreatment, in the absence of rupture after initial treatment, occurred in 42/315 (13.3%) BMC and 40/311 (12.9%) Matrix^2 patients, while sudden unexplained death occurred in 1/315 (0.3%) BMC and 2/311 (0.6%) Matrix^2 patients. No comparisons between BMC and Matrix^2 in the subcomponents of TAR reached statistical significance. Similarly, there was no difference in TAR between the BMC and Matrix^2 groups for the subgroup of patients treated with stents in addition to coiling.

Tar versus angiographic results

For all patients combined (BMC and Matrix^2) the correlation between the core lab adjudicated immediate post-treatment angiographic results and TAR was highly statistically significant (table 1).

Table 1 Contingency table between 5-year target aneurysm recurrence and modified Raymond Scale

Modified Raymond Scale (core lab post-procedure)	1915-day TAR	P value*
Raymond I	10.2% (18/176)	<0.0001
Raymond II	8.6% (11/128)	
Raymond III	25.5% (47/184)	

*Chi-squared across three groups.
TAR, target aneurysm recurrence.

When considering the two treatment groups separately, this correlation was not statistically significant for the BMC patients (P=0.3) but was significant for the Matrix^2 patients (P<0.001) (table 2).

While there was no difference in the TAR rate between the BMC and Matrix^2 groups, and for all patients combined the initial core lab adjudicated occlusion scores were predictive of TAR, the initial Raymond score was more strongly predictive of future TAR in the Matrix^2 group than in the BMC group. This finding appears to be driven by the lower number of Matrix^2 patients going on to have a TAR event if their initial adjudicated Raymond occlusion score was Raymond I or II, a statistically significant difference noted on post hoc analysis (P=0.02, Chi-squared Raymond I and II vs Raymond III). The rate of TAR seen at follow-up in patients with immediate post-treatment Raymond grade I adjudicated occlusion was 5.7% in the Matrix^2 treated patients versus 14.6% for the BMC patients (P=0.05), at the borderline of statistical significance. In other words, Matrix^2-treated patients whose initial angiographic occlusion score was Raymond grade I or II had lower rates of TAR than did Raymond I or II patients treated with BMCs. Conversely, among patients whose initial degree of occlusion was Raymond III, the more frequent occurrence of TAR in the Matrix^2 group did not reach statistical significance (P=0.1, Chi-squared Raymond I and II vs Raymond III).

Aneurysm hemorrhage after treatment

Of the 626 aneurysms treated, 228 aneurysms were acutely ruptured prior to randomization and the remaining 398 had not previously ruptured. Three of the 228 (1.3%) patients presenting with ruptured aneurysms experienced re-hemorrhage in the peri-operative period, that is, after coiling but prior to discharge from hospital (online supplemental table 3). All three of these patients had Raymond III residual aneurysm filling after their initial treatment. After 5 years of follow-up, no additional patients presenting with a ruptured aneurysm are known to have suffered recurrent aneurysmal hemorrhage.

After 5 years of follow-up, two of the 398 patients originally presenting with unruptured aneurysms are known to have had target aneurysm rupture (online supplemental table 3). Both of these patients had large aneurysms (>10 mm), both had core lab adjudicated Raymond III residual aneurysm filling at completion of treatment and both showed aneurysm coil compaction plus aneurysm growth at the representation with hemorrhage. The hemorrhages occurred 344 and 541 days after the initial treatment. For the MAPS trial the annualized rate of known delayed rehemorrhage after coiling was 2 patient-hemorrhages/1515.9 patient-years of follow-up=0.0013 (0.13%) per year for unruptured aneurysms and 0 for previously ruptured aneurysms.

Table 2 Contingency table between 5-year target aneurysm recurrence and modified Raymond Scale by coil type

Raymond Scale (core lab post-procedure)	BMC 1915-day TAR	P value	Matrix^2 1915-day TAR	P value
Raymond I	14.6% (13/89)	0.3*	5.7% (5/87)	<0.0001*
Raymond II	11.8% (8/68)		5.0% (3/60)	
Raymond III	20.4% (19/93)		30.8% (28/91)	
Raymond I	14.6% (13/89)		5.7% (5/87)	0.08†
Raymond II	11.8% (8/68)		5.0% (3/60)	0.2†
Raymond III	20.4% (19/93)		30.8% (28/91)	0.13†

*Chi-squared across three groups (Raymond I, II and III combined, BMC vs Matrix^2).
†Fisher's exact Chi-squared comparing BMC to Matrix^2 within each Raymond group separately (ie, comparison across horizontal rows).
BMC, bare metal coil; TAR, target aneurysm recurrence.

While not part of the predetermined endpoints, it is nonetheless noteworthy that all hemorrhages occurring after treatment involved patients with residual aneurysm filling, that is, Raymond III. The correlation of post-treatment subarachnoid hemorrhage with Raymond III filling versu. combined Raymond I or II occlusion scores is highly statistically significant (P=0.008, logistic regression).

TAR predictors by logistic regression

Logistic regression showed statistically significant predictors of TAR included, in decreasing order of odds of TAR: aneurysm size (>10 mm), rupture status, core lab adjudicated Raymond score (III vs I) and aneurysm neck size (>4 mm) (table 3).

Rupture status and correlation of TAR with post-procedure Raymond Scale

As noted above in the logistic regression analysis, rupture status is highly correlated with retreatment and therefore TAR. As shown in table 4, immediate post-procedure modified Raymond Scale score of III is predictive of TAR regardless of rupture status, but unsurprisingly is more powerfully correlated with TAR in the ruptured cohort. Almost half the patients with ruptured aneurysms and Raymond III initial occlusion went on to retreatment as compared with less than one-fifth of the Raymond III patients in the unruptured cohort. This is even more important when it is noted that immediate post-procedure Raymond III scores were seen in only 23.4% of the ruptured patients but in 45.3% of the unruptured patients. In other words, Raymond III occlusion was much more often accepted as an initial treatment result in the unruptured aneurysms but did not lead to more frequent retreatment at follow-up.

Table 3 1915-Day target aneurysm recurrence predictors by multivariate logistic regression intent-to-treat, all patients

Multivariate – overall (n=626) variable	OR (95% CI)	P value
Dome size (>10 mm vs <10 mm)	6.3 (2.9 to 13.9)	<0.0001
Rupture status (ruptured vs unruptured)	4.0 (2.2 to 7.4)	<0.0001
Raymond Scale 3 vs 1 (core lab post-procedure)	3.6 (1.8 to 6.9)	0.0002
Neck size (≥4 mm vs <4 mm)	2.4 (1.4 to 4.3)	0.003
Raymond Scale 2 vs 1 (core lab post-procedure)	0.9 (0.4 to 2.0)	0.8

CI, confidence interval; OR, odds ratio; TAR, target aneurysm recurrence.

Timing of TAR

The majority of TAR events were asymptomatic retreatments and took place within the first 2 years after treatment. No hemorrhages occurred after the second year. Follow-up imaging was required as part of the study at 1 year but not thereafter. No patient suffered aneurysmal hemorrhage after year 2. Only 4 (0.6%) retreatments took place between years 2 and 3 (online supplemental table 4) and even though 40.8% of patients had follow-up imaging after year 3, none were retreated.

Geography of TAR

As previously reported,[10] TAR rates after the first year were noted to be higher outside of North America, driven by higher rates of asymptomatic retreatment in North America as opposed to elsewhere. By the end of the second year, however, this difference was no longer statistically significant, with retreatment rates of 11.1% in North America versus 13.1% elsewhere, suggesting that retreatment happens later outside of North America, but at a similar rate per patient treated.

DISCUSSION

BMC versus Matrix^2

Very few randomized trials of aneurysm coiling have been published that track patient outcomes beyond 18 months. ISAT and BRAT are the exceptions.[11 12] While the Matrix^2 coil was shown by the primary outcome of this trial to be non-inferior after 5 years of follow-up, no benefit was demonstrated. As noted at the year 1 follow-up, aneurysms initially well occluded had a lower TAR rate with the Matrix^2 coils, whereas there was a balancing trend towards a higher TAR rate for Matrix^2 patients that had an initial post-treatment Raymond score of III.[8] This may be due to a 'threshold' effect where the potential benefit of the Matrix^2 coating is gained only if there is an initial stable occlusion of the aneurysm, or it could be a chance finding.

Despite the past failure of multiple trials to show clinical benefit from coils combined with active polymers, the concept remains attractive. Indeed, a meta-analysis has demonstrated an increased rate of complete angiographic occlusion at mid-term follow-up, as well as decreased Raymond III residual aneurysm filling in the subgroup of patients treated with hydrogel-coated coils.[13] Similarly, the recently published German–French Randomized Endovascular Aneurysm Trial (GREAT) has suggested that second-generation hydrogel coils may reduce the rate of unfavorable outcome events[14] and the final results of the HEAT trial[15] also suggested a benefit to hydrogel coating.

Table 4 Correlation of target aneurysm recurrence with Raymond Scale: ruptured versus unruptured aneurysms

Modified Raymond Scale (core lab post-procedure)	Ruptured 1915-day TAR	P value*	Unruptured 1915-day TAR	P value*
Raymond I	13.3% (11/83)	<0.0001	7.5% (7/93)	0.004
Raymond II	10.4% (5/48)		7.5% (6/80)	
Raymond III	48.8% (20/41)		18.9% (27/143)	

*Fisher exact test of Raymond I and II vs Raymond III for treatment arm.
TAR, target aneurysm recurrence.

Immediate post-treatment Raymond score predicts TAR and aneurysmal hemorrhage

The statistically highly significant correlation observed in MAPS between the core lab adjudicated initial Raymond grade of occlusion and the long-term retreatment and re-hemorrhage rates has not been previously demonstrated in a multicenter randomized trial. As all post-treatment hemorrhages occurred in patients with Raymond III residual aneurysm filling the clear message is that Raymond I and II occlusion patients are at very low risk of delayed hemorrhage and efforts should be made to achieve this level of occlusion. It is reasonable to speculate that the reason that hemorrhages were seen only in the unruptured cohort is related to the fact that Raymond III residuals were more frequently accepted as the end result of the initial treatment and less aggressively retreated at follow-up than was the case for patients who had originally presented with subarachnoid hemorrhage. Of the 398 patients with unruptured aneurysms, 143 patients had core lab adjudicated residual filling of their aneurysm sac (Raymond III). Over 5 years, two hemorrhages occurred in this group of patients versus none in the patients treated with Raymond I or II occlusion (P=0.13). Assuming no additional hemorrhages occurred in patients lost to follow-up, the annual re-hemorrhage rate in the Raymond III patients is: $2/(143 \times 5) \times 100 = 0.28\%$ per year, only slightly better than the natural history.[16] The findings in MAPS are consistent with those of Ogilvy et al correlating retreatment with the Raymond grade of occlusion as well as with aneurysm size and rupture status among other factors.[17]

A legitimate concern is that the correlation between Raymond score and TAR was much stronger for the core lab reported Raymond score than for the self-reported Raymond occlusion score. As in multiple other studies, the self-reported results of angiographic occlusion in MAPS were more favorable than the core lab adjudicated results.[18 19] Accordingly, using self-reported results in daily clinical practice to estimate the risk of TAR for an individual patient should be done with caution.

Timing of retreatments

Another useful finding of MAPS is that the majority of retreatments occurred early in the follow-up period. This was similarly noted in the BRAT trial (C McDougall, personal communication, 2020) There are several possible explanations for this:

- It may suggest that most aneurysms become stable once Raymond I or II occlusion has been achieved;
- It may be that the operators believe they have achieved the best degree of occlusion they could, and therefore do not feel additional retreatment attempts will result in improved occlusion; or
- It may be that some patients no longer return for additional follow-up and retreatment.

This naturally begs the question as to what imaging follow-up should be recommended. Several strategies could be considered in light of the current findings. First, one may conclude that as there are few patients being retreated after 3 years that all patients should be followed with some form of imaging for this length of time, but that beyond 3 years there are too few patients requiring retreatment to justify imaging follow-up for all patients. Alternatively, one may conclude that long-term follow-up is only required for aneurysms with residual filling (Raymond III). Again, since only patients with Raymond III residual aneurysm filling re-bled, it would seem prudent to treat rather than follow such patients if this can be done with acceptable risk. Finally, one may conclude that long-term follow-up is justified for all patients so that any patients who develop Raymond III filling may be identified and retreated. Some longer-term studies, for example Lecler et al, have suggested that particularly for aneurysms larger than 10 mm, there is a significant risk of deterioration from Raymond rade II to Raymond grade III filling between mid-term and 10-year follow-up with retreatment being required even after 10 years in these patients.[20] More recently, clinically inspired models of coiled aneurysms have confirmed that aneurysm morphology, coil packing and post-coiling hemodynamics affect long-term treatment outcome.[21]

While the strength of this trial is the diligent prospective clinical 5-year follow-up in all available patients, the major limitation is that long-term imaging was not mandated beyond the first year, and in practice only 31.7% of the patients had follow-up imaging in year 4 or 5.

CONCLUSIONS

After 5 years Matrix^2 coils were non-inferior to BMCs but no benefit was demonstrated. Residual aneurysm filling (core lab adjudicated Raymond III score) at the completion of the initial aneurysm treatment is highly predictive of TAR (P<0.0001). Rupture of coiled aneurysms was uncommon and was observed only in aneurysms with continued residual filling of the aneurysm dome (Raymond III) after treatment (P=0.008). This trial has demonstrated that angiographic failure, defined as Raymond III residual aneurysm filling after coiling, is highly correlated with clinical failure, defined as TAR and with aneurysmal hemorrhage after treatment. The goal of aneurysm coiling should be Raymond I or II occlusion. Patients with Raymond III residual aneurysm filling should be followed carefully and retreated when clinically appropriate.

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Funding This study was funded by Stryker (MAPS Trial).

Competing interests SWH: core lab services for Stryker and MicroVention Terumo (money paid to UCSF, over $5K); consulting for Microvention Terumo (money paid to Dr Hetts, under $5K). CGM: consultant for Medtronic and Microvention. JCC: consultant for Stryker. AB: consultant for Stryker, Microvention, Balt, and Phenox. AKW: research grant from Philips Medical; serves as a consultant for Stryker and Phenox; is a stockholder of InNeuroCo, EpiEP, Neural Analytics, Rist, Analytics 4 Life, and ThrombX; and is on the Speakers' Bureau for SCENT trial (Surpass Intracranial Aneurysm Embolization System Pivotal Trial to Treat Large or Giant Wide Neck Aneurysms) presentations. AG: consultant for Microvention and emeritus consultant at Newcastle upon Tyne Hospitals NHS Trust. CFD: chief adjudicator, Stryker EVOLVE Trial Core Angiography Lab (salary support to department).

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. All datasets are available upon reasonable request. These data are maintained by Stryker Neurovascular. Patricia Morgan, BSN, RN, Medical Science Liaison, can be contacted at patricia.morgan@stryker.com regarding such inquiries.

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REFERENCES

1 Raymond J, Guilbert F, Weill A, *et al*. Long-term angiographic recurrences after selective endovascular treatment of aneurysms with detachable coils. *Stroke* 2003;34:1398–403.
2 Gómez G, Gómez-Mateu M, Dafni U. Informed choice of composite end points in cardiovascular trials. *Circ Cardiovasc Qual Outcomes* 2014;7:170–8.
3 Molyneux AJ, Clarke A, Sneade M, *et al*. Cerecyte coil trial: angiographic outcomes of a prospective randomized trial comparing endovascular coiling of cerebral aneurysms with either cerecyte or bare platinum coils. *Stroke* 2012;43:2544–50.
4 White PM, Lewis SC, Gholkar A, *et al*. Hydrogel-coated coils versus bare platinum coils for the endovascular treatment of intracranial aneurysms (HELPS): a randomised controlled trial. *Lancet* 2011;377:1655–62.
5 Raymond J, Klink R, Chagnon M, *et al*. Hydrogel versus bare platinum coils in patients with large or recurrent aneurysms prone to recurrence after endovascular treatment: a randomized controlled trial. *AJNR Am J Neuroradiol* 2017;38:432–41.
6 Raymond J, Klink R, Chagnon M, *et al*. Patients prone to recurrence after endovascular treatment: periprocedural results of the PRET randomized trial on large and recurrent aneurysms. *AJNR Am J Neuroradiol* 2014;35:1667–76.
7 Poncyljusz W, Zarzycki A, Zwarzany Łukasz, *et al*. Bare platinum coils vs. HydroCoil in the treatment of unruptured intracranial aneurysms—a single center randomized controlled study. *Eur J Radiol* 2015;84:261–5.
8 McDougall CG, Johnston SC, Gholkar A, *et al*. Bioactive versus bare platinum coils in the treatment of intracranial aneurysms: the MAPS (matrix and platinum science) trial. *AJNR Am J Neuroradiol* 2014;35:935–42.
9 Hetts SW, Turk A, English JD, *et al*. Stent-assisted coiling versus coiling alone in unruptured intracranial aneurysms in the matrix and platinum science trial: safety, efficacy, and mid-term outcomes. *AJNR Am J Neuroradiol* 2014;35:698–705.
10 Turk AS, Johnston SC, Hetts S, *et al*. Geographic differences in endovascular treatment and retreatment of cerebral aneurysms. *AJNR Am J Neuroradiol* 2016;37:2055–9.
11 Molyneux AJ, Kerr RSC, Birks J, *et al*. Risk of recurrent subarachnoid haemorrhage, death, or dependence and standardised mortality ratios after clipping or coiling of an intracranial aneurysm in the International Subarachnoid Aneurysm Trial (ISAT): long-term follow-up. *Lancet Neurol* 2009;8:427–33.
12 Spetzler RF, McDougall CG, Zabramski JM, *et al*. The Barrow Ruptured Aneurysm Trial: 6-year results. *J Neurosurg* 2015;123:609–17.
13 Broeders JA, Ahmed Ali U, Molyneux AJ, *et al*. Bioactive versus bare platinum coils for the endovascular treatment of intracranial aneurysms: systematic review and meta-analysis of randomized clinical trials. *J Neurointerv Surg* 2016;8:898–908.
14 Taschner CA, Chapot R, Costalat V, *et al*. Second-generation hydrogel coils for the endovascular treatment of intracranial aneurysms: a randomized controlled trial. *Stroke* 2018;49:667–74.
15 Bendok BR, Abi-Aad KR, Ward JD, *et al*. The Hydrogel Endovascular Aneurysm Treatment trial (HEAT): a randomized controlled trial of the second-generation hydrogel coil. *Neurosurgery* 2020;86:615–24.
16 Murayama Y, Takao H, Ishibashi T, *et al*. Risk analysis of unruptured intracranial aneurysms: prospective 10-year cohort study. *Stroke* 2016;47:365–71.
17 Ogilvy CS, Chua MH, Fusco MR, *et al*. Validation of a system to predict recanalization after endovascular treatment of intracranial aneurysms. *Neurosurgery* 2015;77:168–74.
18 Rezek I, Lingineni RK, Sneade M, *et al*. Differences in the angiographic evaluation of coiled cerebral aneurysms between a core laboratory reader and operators: results of the Cerecyte coil trial. *AJNR Am J Neuroradiol* 2014;35:124–7.
19 Taki W, Sakai N, Suzuki H, *et al*. Importance of independent evaluation of initial anatomic results after endovascular coiling for ruptured cerebral aneurysms. *J Clin Neurosci* 2013;20:527–31.
20 Lecler A, Raymond J, Rodriguez-Régent C, *et al*. Intracranial aneurysms: recurrences more than 10 years after endovascular Treatment-A prospective cohort study, systematic review, and meta-analysis. *Radiology* 2015;277:173–80.
21 Damiano RJ, Tutino VM, Paliwal N, *et al*. Aneurysm characteristics, coil packing, and post-coiling hemodynamics affect long-term treatment outcome. *J Neurointerv Surg* 2020;12:706–13.